PATENT COOPERATION TREATY

WE

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

NRT2 8-9-2001

PCT

To:

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C/O VEREENIGDE
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TERMIJN
06 JUN 2001
Beantwoord
Voorl.
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Bericht gezonden aan
dd.
MAP

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	29.05.2001
Applicant's or agent's file reference	**IMPORTANT NOTIFICATION**
P22152PC00	

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/NL00/00152	08/03/2000	08/03/1999

Applicant
STICHTING DIENST LANDBOUWKUNDIG ONDERZOEK et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	CLEERE, C Tel.+49 89 2399-8061

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
P22152PC00		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/NL00/00152	08/03/2000	08/03/1999
International Patent Classification (IPC) or national classification and IPC		
C12N15/86		
Applicant		
STICHTING DIENST LANDBOUWKUNDIG ONDERZOEK et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
15/09/2000	29.05.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Bassias, I Telephone No. +49 89 2399 8106

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/NL00/00152

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-41	as originally filed				

Claims, No.:

1-22	as received on	25/04/2001	with letter of	25/04/2001	

Drawings, sheets:

1/4-4/4	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 4, 22.

because:

☒ the said international application, or the said claims Nos. 22 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 4 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1,3; 5-22 (reserved opinion)

	No:	Claims	2
Inventive step (IS)	Yes:	Claims	5-22 (reserved opinion)
	No:	Claims	1-3
Industrial applicability (IA)	Yes:	Claims	1-21
	No:	Claims	-

2. Citations and explanations
see separate sheet

Re Item III

1. The scope of claim 4 is so unclear (Article 6 PCT) that no meaningful opinion could be given for said claim. A replicon of a positive-strand RNA virus comprises anyway RNA, thus such a claim does not further characterize the subject-matter of claims 1-3.

2. For the assessment of the present claim 22 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item V

1. Reference is made to the following document:

   D1: WO 98 55626 A (REILLY JOHN DAVID ;COUSSENS PAUL M (US); ORIGEN INC (US); SPATZ ST) 10 December 1998 (1998-12-10)

2. The amended claims filed with the letter of 25.04.2001 appear to be allowable under Articles 19(2) and 34(2)(b) PCT.

3. Claim 1 relates to a porcine reproductive and respiratory syndrome virus (PRRSV) replicon having at least some of its original PRRSV nucleic acid deleted wherein said replicon **comprises essential elements from the PRRSV polymerase region** and is capable of *in vivo* RNA replication.

   Document D1 refers to a recombinant PRRS virus (and its nucleic acid) wherein the ORFs 2-7 from PRRSV are linked to a **heterologous** polymerase gene in particular to ORFs 1a and 1b from Equine Arteritis Virus (EAV) ("abstract", p.8, l.18-21 and/or p.9, l.16-19). The construction of such a nucleic acid (replicon) is

described in "Example 3" and one possible example of such a replicon is the plasmid p4B, shown in Fig.3B.

The difference between the subject-matter of the present application and D1 is that the replicon of the present application comprises essential elements from the own polymerase region whereas the replicon of D1 comprises the polymerase gene from EAV. Due to this difference the subject-matter of claim 1 appears to be novel over D1 and over the remaining cited prior art documents.

However, the subject-matter of claim 1 lacks an inventive activity (Article 33(3) PCT) for the following reasons:
As mentioned above, the only difference between the replicon of the application and D1 is the origin of the polymerase gene. From the disclosure it is not clear what advantage a replicon which has its polymerase gene would have over a replicon containing a heterologous polymerase gene. Since the intention for the use of the replicon in the present application and D1 is the same, namely to use it for vaccination, it appears that it has even disadavantages over the replicon of D1. According to page 12 (l. 13-15) of D1 the EAV RNA polymerase appears to have an increased fidelity. This property is clearly positive for vaccination purposes. Hence, a replicon having a higher mutation rate for vacciniation against PRRSV appears not to solve any clear technical problem and thus claim 1 is not in accordance to Article 33(3) PCT.

4. Claim 2 which does not relate to a PRRSV replicon comprising its own polymerase gene but merely to a replicon comprising nucleic acid derived from at least one heterologous micro-organism lacks even novelty over D1 (Article 33(2) PCT). The PRRSV replicon of D1 having the polymerase gene of another virus, namely EAV falls within the scope of claim 2.

5. The available prior art appears not to disclose that the 5' noncoding region-ORF1a-ORF1B-ORF7-3' noncoding region is essential for *in vivo* RNA replication. Furthermore, replicons having mutations in the gene encoding the M-protein or modifications leading to amino acid changes in ORF2, 3, 4, 5 and/or 6 or modifications in a virulence marker of PRRSV are also not described or suggested in the cited prior art. Hence, claims relating to said subject-matter, i.e., claims 5-9

and 11-15 would be in accordance to Article 33(2) and (3) PCT if they would not refer to claim claims 1-4.

6. Claims 10 and 16-22 referring to the replicon as specified in claims 1-4 do not satisfy the requirements of Article 33(2) and/or (3) PCT. D1 describes also recombinant PRRSV containing a marker which allows the identification of the recombinant PRRSV (p.16, l.1-6). The recombinant virus/replicon of D1 contains nucleic acid parts derived from EAV which is a pathogenic virus for horses. Furthermore, it is stated in D1 that the described nucleic acid constructs are used to produce a vaccine for protecting swine from infection by PRRSV (p.9, l.1-3 and claim 41).
Claims 10 and 16-22 would only be in accordance to Article 33(2) and (3) PCT if they would restrict to replicons characterised with specific technical features which are not known from the prior art, e.g. replicons as defined in claims 5, 6, 8, 9 and 11-15.